REMARKS

Claim Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejects claims 1-19, 43-44, 47-51, 54-60, 63, 65, and 67-68 and asserts that there is a lack of enablement for the treatment of diseases, other than specific types of cancer (e.g., colon cancer), encompassed by those claims.

The first aspect of this rejection relates to claims drawn to "a method of inhibiting ERK2 activity in a patient." Those claims are 1-9, 19, 43, and 44. In order to expedite prosecution, Applicants cancel claims 43 and 44 and amend claims 1 and 19 to recite the specific diseases associated with the inhibition of ERK2 in a patient. Specifically, Applicants amend claim 1 to recite "A method of treating transplant rejection, melanoma, or a cancer selected from colon, breast, lung, kidney, ovary, pancreas, CNS, or cancer of the gastric tract, in a patient ... ." Because claims 2-9 depend upon claim 1, these claims are rendered enabled by this amendment of claim 1.

Applicants respectfully submit that claim 10, and claims 11-18 dependent thereon, relate not to the inhibition of ERK2 activity in a patient but to the inhibition of ERK2 in a biological sample. These claims 10-18 do not relate to the treatment of any disease in a patient. Accordingly, Applicants respectfully request that the Examiner withdraw his rejection of claims 10-18. In light of the forgoing, Applicants respectfully request that the Examiner withdraw his rejection of claims 1-19, 43, and 44.

The second aspect of this rejection relates to claims drawn to "a method of treating a disease in a patient ..." followed by a list of disorders. Those claims are 47-51, 54-60, 63, 65, and 67-68. In order to expedite prosecution, Applicants cancel claims 47 and 48. In response to the Examiner's rejection, applicants respectfully submit that claims 58-60 and 68 do not relate to the treatment of diseases, *per se*. Specifically, claim 68 relates to the inhibition of ERK2, Aurora-2, GSK-3, CDK-2, AKT3, or Lck activity in a biological sample. Furthermore, claims 57-60 relate to the effects of inhibiting ERK2, Aurora-2, GSK-3, CDK-2, AKT3, or Lck activity in a patient. Accordingly, Applicants respectfully request that the Examiner withdraw his rejection of claims 57-60 and 68.

Regarding the Examiner's rejection of claims 49-51, 54-56, 63, 65, and 67, Applicants respectfully traverse. Claims 49-51, 54-56, 63, and 65 relate to specific diseases associated with the protein kinases inhibited by the compounds of the present invention. Applicants respectfully submit that each of the recited diseases is, in fact, enabled by the specification. Specifically, applicants point out that the background section of the above-identified

application describes a nexus between the inhibition of the recited protein kinases with the treatment of the various diseases recited. This nexus has been demonstrated in both *in vitro* and *in vivo* models. *See* pages 1-5. As stated in the MPEP, "if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the Examiner has evidence that the model does not correlate." See MPEP § 2164.02. Because the models cited in the background section of the present application do correlate the inhibition of the protein kinases recited therein with the treatment of the various diseases recited by the claims and because the Examiner has not provided evidence that these models do not correlate the inhibition of these protein kinases with the treatment of the recited diseases, applicants respectfully submit that claims 49-51, 54-56, 63, and 65 are indeed enabled.

Furthermore, enablement requires the applicant to provide sufficient guidance so that one of skill in the art may use the invention. The MPEP states that "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." See MPEP §2164.06. Applicants do in fact provide the tools to make the compounds of the instant invention and assess the activity of those compounds. For example on page 77, line 1 through page 87, line 14 applicants provide specific procedures for the preparation of the compounds of the present invention and on page 119 through page 124 applicants provide methods for assaying the present compounds as inhibitors of ERK2, Aurora-2, GSK-3, CDK-2, AKT3, and Lck protein kinases.

The Examiner further asserts that although the inhibitory data for some compounds of the present invention is provided in the specification there is no disclosure correlating this data to the treatment of the diverse disorders of the instant claims. Applicants respectfully traverse. Specifically, applicants respectfully point the Examiner towards the numerous literature references recited in the background section of the specification which correlate each kinase target with the diseases associated thereto.

The Examiner states that factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. Applicants respectfully traverse. First, applicants respectfully submit that working examples are not required by U.S.C. § 112, first paragraph. See MPEP § 2164.02. Also, Applicants respectfully point out that the models cited in the background section of the present application do correlate the inhibition of protein kinases with the diseases recited by the instant claims, as described *supra*. See MPEP § 2164.02.

Furthermore, the court in *In re Brana*, 52 F.3d 1560 (Fed. Cir. 1995) reversed the PTO decision that *in vitro* data did not support *in vivo* applications. Additionally, only a "reasonable correlation" is required, and the test does not have to be "highly predictive" as the Examiner suggests. Additionally, Applicants would like to point out that each of the rejected claims recites *treating* of certain diseases, or conditions, and does not recite the *reversal* of diseases such that a "magic bullet" is within the scope of the instant claims.

In light of *Brana* and the various sections of the MPEP cited herein, the *in vitro* data and methods do support the *in vivo* applications of the instant claims. Thus, applicants respectfully submit the above arguments and amendments and request that the Examiner acknowledge sufficient enablement of claims 49-51, 54-56, 63, and 65.

Claim Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejects claim 20, and claims dependent thereon as being indefinite. As suggested by the Examiner, Applicants amend claim 20 to replace the term "comprising" in the definition of Sp with the term "having". Applicants also amend claims 1 and 10 in the same fashion. In light of this amendment, Applicants respectfully request that the Examiner withdraw his rejection of claims 20, 41-42, 49-51, 54-60, 63, 65, and 67-70.

Claim Rejections Under Obviousness-Type Double Patenting

The Examiner provisionally rejects claims 20-31, 41-43, 47-51, 54-56, 63, 65, and 67-70 as being unpatentable over claims 1-35 of copending application 10/121,035 and asserts that the instant claims overlap the reference compounds. Applicants respectfully traverse and submit that the instant claims are outside the scope of the reference claims. Specifically, the reference relates to pyrimidinyl compounds having a thienyl group at the 4-position as do the instant compounds when Sp is thienyl. However, the instant compounds differ from the reference compounds because the reference compounds require substitution at every position of the thienyl ring, *i.e.* no hydrogen atoms at any position of the thienyl ring. In contrast, the instant compounds require at least one unsubstituted position on the Sp ring. Specifically, the present invention defines the Sp group as follows:

> "Sp is a spacer group comprising a 5-membered heteroaromatic ring, wherein Ring A and QR^2 are attached to Sp at non-adjacent positions; and wherein Sp has up to two R^6 substituents, **provided that two substitutable carbon ring atoms in Sp are not simultaneously substituted by R^6**;" (emphasis added).

Accordingly, because the present invention does not overlap with the reference compounds, Applicants respectfully request that the Examiner withdraw his provisional rejection of claims 20-31, 41-43, 47-51, 54-56, 63, 65, and 67-70.

Applicants believe that no additional fees are due at this time however, the Commissioner is hereby authorized to charge payment of additional fees required in connection with the paper transmitted herewith, or credit any overpayment of same, to Deposit Account No. 50-0725.

None of these amendments adds new matter.

Respectfully submitted,

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